Author's response to reviews

Title: Assessment of insulin resistance by a 13C glucose breath test: a new tool for early diagnosis and follow-up of high-risk patients

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Author's response to reviews: see over
The Nutrition Journal Editorial Team

Dear Sir,

RE: MS: 1514406170306620 - Assessment of insulin resistance by a 13C glucose breath test: a new tool for early diagnosis and follow-up of high-risk patients

Thank you for your letter regarding the above manuscript.

Please find enclosed our revised manuscript for your review. The authors appreciate the comments offered by the reviewers. The manuscript has been revised, taking into account the points made in the critique. We believe that the manuscript has been improved as a result of these revisions and hope that it will be acceptable for publication in The Nutrition Journal.

Sincerely yours,

Yaron Ilan, M.D.
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Response to Reviewer 1

1. The data analysis and presentation are totally confusing. What do the points in figures 1-4 represent? Are they individual time points in an individual? If so, they should be identified and labelled as such. More importantly, however, is the point of the 4 figures. If the purpose of this study was to assess the suitability of the described GBT as a measure of insulin resistance, then results of the GBT, however determined, should have been compared with comparable results of other measures of insulin resistance, not with glucose or insulin values from individual time points. Such results are meaningless. Similarly, carrying out correlation or regression analysis, within subjects, is also virtually meaningless - it stands to reason that higher blood glucose levels would be inversely correlated with breath results. Rather, the authors should correlate results of all 20 subjects using GBT parameters as one variable and other measures of insulin resistance as the second variable. The analysis must be completely re-done. Not that there may not be significant results, but the current results don't mean anything.

We accept the comment. The statistical analysis was performed as suggested by the reviewer. In addition to individual examples, an analysis on all patients enrolled was performed comparing the results of the tests with insulin and glucose levels and with HOMA IR/B. The relevant paragraphs in the Results and in the Discussion were revised accordingly. Two figures were added to the manuscript to provide the analysis as requested by the reviewer.

2. In keeping with the point above, exercise as a mechanism to reduce insulin Resistance should be assessed by single GBT variables and compared to other methods of insulin resistance. In other words, how did exercise change the variable compare to e.g. HOMA 90? Correlation as presented here is meaningless as well.

We accept the comment. However, in light of the small number of participants, a comparison with all parameters is of limited significance. We have revised the relevant sections in the results and discussion sections.

Minor Essential Revisions

1. It is unclear how correlations were done. For example, comparing HOMA B
120 to CPDR 30 leads me to believe a correlation matrix was constructed. Thus, how were multiple, repetitive correlations statistically handled to rule out chance? (i.e. the correlative equivalent of multiple comparisons)

We accept the comment. The association between two variables was assessed by calculating the Pearson and the Spearman correlation coefficients. Calculations of the within-subjects correlation coefficients between each pair over all subjects were derived from an analysis of variance table in a General Linear Model, or from the within-cell correlations in Multivariate Analysis of Variance (ANOVA). The relevant sections were revised to clarify this point.

2. In section 2.2, 3rd last sentence, "frequently determined" should be defined
   Corrected as suggested by the reviewer.

3. The difference between PDR and CPDR should be better explained in 2.3
   The relevant section was revised.

4. The meaning of the second sentence of 2.3 is unclear
   Revised as suggested.

5. The entire 3.6 section is unclear
   We have revised the section as suggested.

6. Why is HOMA B 120 correlated with CPDR 30? What is the rationale for doing this comparison vs the logical 120 vs 120 comparison?
   We accept the comments. In order to determine a possible correlation that can enable a use of a short term breath test to detect early diabetes a correlation of HOMA 120 with CPDR 30 was performed. This may enable to predict the levels of insulin and glucose at 120 minutes and OGGT after 30 minutes of GBT.

7. The authors need to be careful about the use of R vs r when indicating correlation
   Corrected in all relevant sections of the new version of the manuscript.
8. The results are NEGATIVELY correlated; the authors' use of the term "correlated" implies a positive correlation. We accept the comment, and it was corrected throughout the manuscript.

Statistical Review - authors must address minor essential revision #1
Corrected as requested

Level of interest: An article of importance in its field
Quality of written English: Acceptable